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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
COLLINS, CYNTHIA E	

ART UNIT	PAPER NUMBER
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/732,439	ANDERSON ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *59-96* is/are pending in the application.

4a) Of the above claim(s) *64-71 and 74-96* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59-63,72 and 73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Appeal Brief filed March 15, 2004 has been entered.

The amendment after final rejection filed on 15 March 2004 has been entered.

The finality of the office action mailed September 9, 2003 is hereby withdrawn.

Claim 73 is newly amended.

Claims 59-96 are pending.

Claims 64-71 and 74-96 are withdrawn from consideration.

Claims 59-63 and 72-73 are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Claim Objections

Claim 72 is objected to because it depends upon nonelected claim 66. Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 59-63 and 72-73 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the office action mailed September 9, 2003.

Applicants' arguments filed March 15, 2004, have been fully considered but they are not persuasive.

Applicants argue that given the art known status of proline-encoding genes, Applicants were in full possession of the genus (brief page 5). Applicants note that genes encoding enzymes that elevate the level of proline were known in the art at the time of filing, and point in particular to Verma et al. (U.S. Patent 5,344,923, Exhibit A), cited in the prior art rejection, which discloses the isolation of a mothbean cDNA clone encoding a bifunctional enzyme, delta^{1}-pyrroline-5-carboxylate synthetase, which is involved in the biosynthesis of proline in plants, and Hu et al. (Proceedings National Academy of Science 89:9354-9358; Exhibit B), which discloses a soybean homologue of delta^{1}-pyrroline-5-carboxylate synthetase, as well as the fact that the enzyme catalyzes the first two steps in proline biosynthesis in plants. Applicants also point to Verbruggen et al., (Plant Physiol. 103(3):771-81 (Nov, 1993)), who teach that pyrroline-5-carboxylate reductase encodes the enzyme that catalyzes the last step of the proline biosynthetic pathway and who describe the cloning of the corresponding gene from *Arabidopsis*. Applicants further point to additional examples of pyrroline-5-carboxylate reductases that have been described, including the human gene (Dougherty et al. J Biol. Chem., 267 (2), 871-875 (1992)) and yeast gene (Brandriss et al. J Bacteriol. 174 (15), 5176 (1992)). Applicants argue that since the sequences were known to those of skill in the art at the time of filing, Applicants cannot be said to lack written description for these sequences. Applicants also argue that a person of ordinary skill in the art would have known of useful gene sequences involved in the synthesis of proline at the time of Applicants' invention, and that the availability of such gene sequences as common knowledge obviates the rejection under 35 USC 112, first paragraph. (brief pages 6-7).

That some genes encoding enzymes involved in proline biosynthesis were known in the art at the time of filing does not demonstrate that Applicants were in full possession of the claimed genus, or that Applicants' disclosure describes the claimed invention sufficiently to satisfy the written description requirement.

First, the claim limitation "recombinant DNA segment encoding an enzyme which catalyzes the synthesis of the osmoprotectant proline", when considered in isolation, would encompass DNA of any sequence obtained from any source and encoding any enzyme of any type and which catalyzes the synthesis of the osmoprotectant proline. The specification does not describe or make reference to even a single such DNA segment or enzyme. Furthermore, the prior art of record does not establish that so broad a genus of sequences had been described in the art at the time of filing. Neither Applicants' specification nor the prior art identify any conserved sequences within the broad genus of any proline biosynthetic enzyme or any gene encoding it, wherein such conserved sequences are correlated with the involvement in proline biosynthesis. See MPEP 2163.

Second, the rejected claims are not solely directed to genes encoding enzymes involved in proline biosynthesis. The rejected claims are directed to transformed plants that are substantially tolerant or resistant to a reduction in water availability, the cells of which comprise a recombinant DNA segment encoding an enzyme which catalyzes the synthesis of the osmoprotectant proline wherein the enzyme is expressed in an amount effective to confer tolerance or resistance to a reduction in water availability. Accordingly, the claims require not simply that the genes encode enzymes involved in proline biosynthesis, but the claims additionally require that the genes encode enzymes that have the capacity to be expressed in a

plant in an amount effective to confer tolerance or resistance to a reduction in water availability. The specification does not indicate which genes encoding which enzymes would have this capacity.

Third, with respect to Verma et al. (U.S. Patent 5,344,923, Exhibit A) and Hu et al. (Proceedings National Academy of Science, October 1992, 89:9354-9358; Exhibit B), both initially cited by the examiner, as well as Dougherty et al. (J Biol. Chem., 267 (2), 871-875 (1992)) and Brandriss et al. (J Bacteriol. 174 (15), 5176 (1992)), their disclosure of two sequences encoding delta^{1}-pyrroline-5-carboxylate synthetase obtained from mothbean and soybean and two sequences encoding pyrroline-5-carboxylate reductase obtained from humans and yeast does not serve to adequately describe the claimed invention, because the disclosure of four sequences encoding two type of enzymes involved in proline biosynthesis is not representative of the genus of sequences used to make the claimed transgenic plant, said sequences having been obtained from any source and encoding any enzyme of any type which catalyzes the synthesis of the osmoprotectant proline, and said sequences further encoding enzymes having the capacity to be expressed in a plant in an amount effective to confer tolerance or resistance to a reduction in water availability.

Fourth, with respect to Appellants' citation of Verbruggen et al. (Plant Physiol. 103(3):771-81 (Nov, 1993)), the disclosure of Verbruggen et al. does not serve to adequately describe the claimed invention because Verbruggen et al. was published after the effective filing date of the instant application (August 1993).

Claims 59-63 and 72-73 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record set forth in the office action mailed September 9, 2003.

Applicants' arguments filed March 15, 2004, have been fully considered but they are not persuasive.

Applicants assert that the claims are fully enabled by the specification, and specifically assert that, as described in the specification, Applicants ' method for transformation of monocots, combined with known examples of enzymes that synthesize the osmoprotectant proline, enables a person of ordinary skill in the art to produce transgenic monocots that express enzymes that synthesize proline (brief page 8).

The Examiner maintains that the specification does not provide even a single example of an enzyme that synthesizes the osmoprotectant proline, or sequences encoding such enzymes. Furthermore, the invention is not limited to transgenic monocots that express enzymes that synthesize proline. The rejected claims are directed to transformed plants that are substantially tolerant or resistant to a reduction in water availability the cells of which comprise a recombinant DNA segment encoding an enzyme which catalyzes the synthesis of the osmoprotectant proline wherein the enzyme is expressed in an amount effective to confer tolerance or resistance to a reduction in water availability. Accordingly, the claims do not simply require that the transgenic monocots express enzymes that synthesize proline. The claims further require that the transgenic monocots express enzymes that have the capacity to be expressed in a plant in an amount

effective to confer tolerance or resistance to a reduction in water availability, which implies that expression of the enzymes would additionally result in increased synthesis and accumulation of proline. This requirement is significant in that the enablement rejection is predicated on the unpredictability of the ability of a recombinant DNA encoding a single enzyme involved in proline biosynthesis to confer tolerance or resistance to a reduction in water availability. Significantly, the specification does not indicate which enzymes involved in the metabolic pathway that synthesizes the osmoprotectant proline have the capacity to actually increase the synthesis of proline when their activity is increased or introduced, and thereby confer tolerance or resistance to a reduction in water availability, and which do not.

Applicants further point out that the currently claimed invention forms a part of a larger invention comprising use of compatible osmoprotectants in monocots in order to achieve resistance to a reduction in water availability. Applicants point out, for example, that they have illustrated this in the context of transgenic plants that express the osmoprotectant mannitol (see US Patent 5,780,709, Exhibit D) and glycine betaine producing enzymes (see U.S. Patent 6,281,411, Exhibit C) (brief page 8).

With respect to US Patent 5,780,709, Exhibit D, and U.S. Patent 6,281,411, Exhibit C, the Examiner maintains that the cited patents are not germane to the instant rejection because each application is examined on its own merits, because the rejected claims are not directed to the use of recombinant DNA molecules encoding mannitol producing enzymes or glycine betaine biosynthetic enzymes, and because the osmoprotectants mannitol, glycine betaine and proline are distinct compounds that are produced by the activities of different sets of

biosynthetic enzymes. The instant enablement rejection is predicated only on the unpredictability of the ability of a recombinant DNA encoding a single unspecified enzyme involved in proline biosynthesis to actually confer tolerance or resistance to a reduction in water availability.

Applicants point out that proline, like mannitol and glycine betaine, is a known endogenous osmoprotectant and has long been identified as playing a role in plants under water deficit. Applicants point in particular to Barnett et al. (Plant Phys., 41:1222, 1966; Exhibit E), who describe that under water deficit, significant increases in certain amino acid pools, such as proline, are observed; to Wyn Jones and Storey (Physiology and Biochemistry of Drought Resistance in Plants, Chapter 9, p. 171-204, Academia Press, Australia, 1981; Exhibit F), who note that increased proline accumulation is observed in barley subjected to water or salt stress; to McCue and Hanson (TIBTECH, 8:358-362, 1990; Exhibit G), who specifically mention the amino acid proline as an osmoprotectant found in diverse organisms; and to Van Rensberg et al. (J. Plant. Physiology, 141:1880194, 1993; Exhibit H), who discuss their observations of increased proline accumulation in drought-resistant tobacco cultivars, where a substantial amount of proline was found to accumulate in the drought-resistant cultivars compared to the drought-sensitive cultivars (brief pages 8-9).

The Examiner does not dispute Applicants' assertion that proline has long been identified as playing a role in plants under water deficit. Furthermore, the Examiner maintains that Applicants' discussion of the role of proline accumulation in plants under water deficit is not germane to the instant enablement rejection, because the rejection is not predicated on the role of proline accumulation in plants under water deficit. The instant enablement rejection is predicated

only on the unpredictability of the ability of a recombinant DNA encoding a single unspecified enzyme involved in proline biosynthesis to actually confer tolerance or resistance to a reduction in water availability.

Applicants argue that their teaching that increased mannitol and glycine betaine impart water stress tolerance to transgenic monocot plants (see US Patent 5,780,709 Exhibit D and US Patent 6,28 1,411 Exhibit C, respectively), and success in using the mtlD gene to impart drought tolerance to a monocot, are therefore indicative of success in overexpressing proline to obtain water stress tolerance. Applicants further argue that together, the knowledge of proline accumulation in plants in response to drought stress, as well as the knowledge of sequences involved in the sequences of proline, demonstrate that the claims were enabled for expressing a proline biosynthesis gene and increased water stress tolerance (brief page 9).

The Examiner maintains that the cited patents teaching that increased mannitol and glycine betaine impart water stress tolerance to transgenic monocot plants are not indicative of success in overexpressing proline to obtain water stress tolerance, because the rejected claims are not directed to increasing mannitol and glycine betaine through the use of recombinant DNA molecules encoding mannitol producing enzymes or glycine betaine biosynthetic enzymes. The rejected claims are also not merely directed to overexpressing proline per se. The rejected claims are directed to increasing proline content in a plant by increasing the expression of proline biosynthetic enzymes by using recombinant DNA molecules encoding proline biosynthetic enzymes to transform plants. The Examiner also notes that the mtlD gene used to impart drought tolerance to a monocot plant encodes an enzyme involved in mannitol biosynthesis, not proline

biosynthesis. The use of the mtlD gene to impart drought tolerance to a monocot plant is therefore not relevant to the enablement of the rejected claims, as mannitol and proline are distinct compounds that are produced by the activities of different sets of biosynthetic enzymes. The Examiner further maintains that the specification provides no guidance with respect to which sequences involved in the synthesis of proline to express in a transformed plant in order to increase proline content and water stress tolerance.

Applicants additionally point out that the Examiner's own prior art rejection states that expression of a delta^{1}-pyrroline-5-carboxylate synthetase would inherently result in water stress tolerance, and Applicants argue that given that the transformation methods and expression vectors illustrated in Appellants' working examples are fully enabled for monocot transformation and heterologous expression with osmoprotectant genes, it is respectfully submitted that the claims must be held enabled in view of the Examiner's assertion. Applicants further argue that while legally flawed from an inherency rejection standpoint because the cited references are not enabling for transgene expression in maize, and the insufficiency of Verma as of its effective date, the art rejection affirmatively acknowledges the enablement of the claims given Applicants' enablement of transgene expression in monocots (brief page 9).

The Examiner does not dispute that Applicants are generally enabled for monocot transformation and heterologous gene expression in monocotyledonous plants. However, the claims are not directed to mere heterologous gene expression in monocotyledonous plants, or specifically to the expression of delta^{1}-pyrroline-5-carboxylate synthetase in monocotyledonous plants. The rejected claims are directed to transformed monocot plants that are substantially

tolerant or resistant to a reduction in water availability the cells of which comprise a recombinant DNA segment encoding any enzyme which catalyzes the synthesis of the osmoprotectant proline wherein the enzyme is expressed in an amount effective to confer tolerance or resistance to a reduction in water availability. Accordingly, the claims do not simply require that the transgenic monocots plants express a heterologous gene. The claims further require that the transgenic monocots express enzymes encoded by heterologous genes wherein the enzymes have the capacity to be expressed in a plant in an amount effective to confer tolerance or resistance to a reduction in water availability, which implies that expression of the enzymes would additionally result in increased synthesis of proline. Furthermore, the instant enablement rejection is not predicated on the availability or predictability of methods for expressing a heterologous gene in monocotyledonous plants. The instant enablement rejection is predicated on the general unpredictability of the ability of a recombinant DNA encoding a single unspecified enzyme involved in proline biosynthesis to confer tolerance or resistance to a reduction in water availability to a transgenic plant, i.e. to result in increased synthesis and accumulation of proline in a transgenic plant. Accordingly the Examiner's assertion that a monocot transformed with the delta^{1}-pyrroline-5-carboxylate synthetase gene would inherently have a resistance to water availability is not tantamount to acknowledging the enablement of the rejected claims, because the rejected claims are not limited to a monocot transformed with the delta^{1}-pyrroline-5-carboxylate synthetase gene, and because the enablement rejection is predicated on the general unpredictability of the ability of a recombinant DNA encoding a single unspecified enzyme involved in proline biosynthesis to confer tolerance or resistance to a reduction in water availability to a transgenic plant. In this regard the Examiner also notes that none of Applicants '

working examples exemplify the effect of expressing in monocots heterologous genes encoding even the single enzyme delta[1]-pyrroline-5-carboxylate synthetase, or the effect of expressing in monocots heterologous genes encoding any other enzyme involved in proline biosynthesis. With respect to the allegedly inconsistent rejections under 35 U.S.C. 112 and 35 U.S.C. 103, the Examiner maintains that the test for adequacy of a prior art disclosure to anticipate or render claims obvious is not the same test as that for adequacy of a patent application disclosure to support claims under 35 U.S.C. 112. See In re Hafner, 161 USPQ 783, (CCPA 1969).

Applicants argue that the Examiner has rejected the claims for lack of enablement based on an alleged failure to disclose the identification or isolation of a particular gene and/or plant comprising recombinant DNA encoding an enzyme involved in proline synthesis. Applicants assert that their method for transformation of monocots combined with known examples of enzymes that catalyze synthesis of the osmoprotectant proline enable a person of ordinary skill in the art to produce transgenic monocots that express these enzymes. Applicants point to their general demonstration that expression of an osmoprotectant in monocots results in water stress tolerance (e.g., Exhibit C and Exhibit D). Applicants point further to numerous lines of evidence that illustrate that proline was well known to be an osmoprotectant (Exhibits E, F, G and Exhibit H). Applicants assert that they have therefore affirmatively set forth evidence of enablement, yet the Examiner has failed to present objective evidence supporting a reasonable doubt of enablement (brief page 5).

With respect to the basis for rejecting the claims for lack of enablement, the Examiner maintains that the enablement rejection is predicated on the general unpredictability of the ability

of a recombinant DNA encoding a single unspecified enzyme involved in proline biosynthesis to confer tolerance or resistance to a reduction in water availability. In this regard the Examiner notes that while disclosure of the identification or isolation of a particular gene and/or plant comprising a recombinant DNA encoding an enzyme involved in proline synthesis is one means by which the specification could provide guidance with respect to which recombinant DNA encoding which enzyme involved in proline biosynthesis to express, such guidance could also be otherwise provided. The issue with respect to the instant case is that the specification provides no guidance at all, for even the isolation of a single gene encoding a single enzyme involved in proline biosynthesis, plant transformation therewith, or successful expression thereof to effectively confer drought tolerance.

As discussed previously, the rejected claims require more than that the transgenic monocots merely express enzymes involved in proline biosynthesis. The claims further require that the transgenic monocots express proline biosynthetic enzymes having the capacity to be expressed in a plant in an amount effective to confer tolerance or resistance to a reduction in water availability, which implies that expression of the enzymes would additionally result in increased synthesis and accumulation of proline. The Examiner maintains that the specification provides no guidance with respect to which enzymes would increase proline content and water stress tolerance upon increased expression in a transformed plant. Applicants' assertions that any gene encoding any enzyme would work, particularly in view of Applicants' failure to provide even a single working example of their broadly claimed genus, are inadequate to overcome the scientific reasoning set forth by the Examiner.

With respect to the teachings of Exhibit C and Exhibit D regarding the use of recombinant DNA molecules encoding mannitol producing enzymes or glycine betaine biosynthetic enzymes, as discussed above Exhibit C and Exhibit D are not considered germane to the instant enablement rejection because mannitol, glycine betaine and proline are distinct compounds that are produced by the activities of different sets of biosynthetic enzymes, and because the instant enablement rejection is predicated only on the unpredictability of the ability of a recombinant DNA encoding a single unspecified enzyme involved in proline biosynthesis to confer tolerance or resistance to a reduction in water availability. With respect to numerous lines of evidence illustrating that proline was well known to be an osmoprotectant, the Examiner does not dispute Applicants' assertion that proline has long been identified as playing a role in plants under water deficit, as discussed previously above, and at page 6 of the office action mailed September 9, 2003. The mere provision of this knowledge to the skilled artisan, however, is not sufficient to enable claims directed to plant transformation with a gene encoding a single unspecified enzyme involved in proline biosynthesis.

With respect to objective evidence supporting a reasonable doubt of enablement, the Examiner asserted at page 6 of the office action mailed November 19, 2002 that the ability of a recombinant DNA encoding an enzyme involved in proline biosynthesis to confer tolerance or resistance to a reduction in water availability is unpredictable, since this ability would be limited by the cellular environment in which the enzyme is expressed. It was further asserted that enzymatic function would be affected by the amount of enzyme expressed, the availability of substrate, and the presence or absence of other factors that might affect enzyme activity or the accumulation of proline.

For example, Delauney et al. teach that multiple enzymes participate in the synthesis of proline in a single biosynthetic pathway in plants and in bacteria, and that proline is also synthesized by two alternative biosynthetic pathways in plants (The Plant Journal, 1993, Vol. 4, No. 2, pages 215-223, page 217 Figures 1 and 2). The participation of multiple enzymes in proline biosynthesis could limit the ability of a single enzyme which catalyzes proline synthesis to produce sufficient proline to confer tolerance or resistance to a reduction in water availability in a plant, since increasing the level of proline in a plant transformed with a transgene encoding a single proline biosynthetic enzyme would depend on the increasing the level of an enzyme that is rate-limiting for proline synthesis. The presence of alternative proline biosynthetic pathways in plants could also limit the ability of a single enzyme which catalyzes proline synthesis to produce sufficient proline to confer tolerance or resistance to a reduction in water availability in a plant, since increasing the level of proline in a plant transformed with a transgene encoding a single proline biosynthetic enzyme would also depend on the amount of enzymatic substrate available, which substrate availability could vary depending on the proline biosynthetic pathway in which the substrate participates. Furthermore, even if proline biosynthesis were increased by the manipulation of one biosynthetic pathway, the proline product produced could act as a feedback inhibitor for the second biosynthetic pathway, so that the total amount of proline produced as the sum of the products of the two pathways might not be sufficient to confer tolerance or resistance to a reduction in water availability in a plant.

Because the ability of a recombinant DNA encoding a single enzyme involved in proline biosynthesis to confer tolerance or resistance to a reduction in water availability, i.e. to cause proline to accumulate, can be affected by multiple uncontrolled variables, and because different

enzymes involved in proline biosynthesis can be affected in different ways by different variables, it is unpredictable whether the expression in a transgenic plant of a recombinant DNA encoding any single unspecified enzyme obtained from any unidentified source that is involved in an unspecified manner in proline biosynthesis would confer tolerance or resistance to a reduction in water availability, i.e. cause proline to accumulate, in a transgenic plant.

Claims 61-63 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons of record set forth in the office action mailed September 9, 2003.

Applicants' arguments filed March 15, 2004, have been fully considered but they are not persuasive.

Applicants reiterate the text of claim 61, with emphasis on its recitation of the term "increased". Applicants argue that the meaning of the term "increased" is clear to one of skill in the art, particularly when taken in combination with the teaching in the specification, and that a plain reading of the claim indicates that the enzyme is increased relative to a *Zea mays* plant that lacks the recombinant DNA segment. Applicants assert that no other logical reading can be made of the claim given the text of the claim, and that the Examiner has failed to point to any other reasonable meaning that could be given. Applicants further assert that there is no indefiniteness in using a relative term that has a comparative basis, and that all that is required under the second paragraph of 112 is that one of skill in the art understand the metes and bounds of the claim when read in context and in view of the specification, and that claim terms must be read together

with the claim as a whole and in view of the understanding of those of skill in the art (brief page 10).

The Examiner maintains that "increased" is a relative term, and that the rejected claim recites no comparative basis for this term. Claims 61, directed to a fertile transgenic *Zea mays* plant, recites that the first DNA segment is expressed so that the level of the enzyme is increased in the transgenic *Zea mays* plant. The Examiner does not dispute that a plain reading of the claim could indicate that the enzyme is increased relative to a *Zea mays* plant that lacks the recombinant DNA segment. When taken in combination with the teaching in the specification, however, a plain reading of the claim could also indicate that the enzyme is increased relative to the level of the endogenous enzyme in the transgenic *Zea mays* plant, or relative to the level of the enzyme produced under non-stress conditions, since the specification does not specifically explain in what way the level of an enzyme which catalyzes the synthesis of the osmoprotectant proline would be increased, and since the specification indicates that one of the mechanisms employed by nontransgenic water deficient-tolerant plants to grow and yield is osmotic adjustment thorough the increased synthesis of osmoprotective metabolites such as proline. Because the rejected claim recites no comparative basis for "increased", and because "increased" could reasonably be interpreted in more than one way when taken in combination with the teaching in the specification, the Examiner maintains that claim 61, and claims 62-63 dependent thereon, are indefinite in the recitation of "increased".

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 63 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 63 is directed to "a seed" produced by the transgenic plant of claim 61, but is not limited to a seed that comprises the recombinant DNA segment that was introduced into the parent plant. Due to Mendelian inheritance of genes, a single gene introduced into the parent plant would only be transferred to half of the seeds of that plant. In addition, given that there is no indication that there would be any other distinguishable characteristics of the claimed seed, it is unclear whether the claimed seed would be distinguishable from seed that would occur in nature. See *Diamond v. Chakrabarty,* 447 U.S. 303 (1980), *Funk Bros. Seed Co. V. Kalo Inoculant Co.*, 233 U.S. 127 (1948), and *In re Bergey,* 195 USPQ 344, (CCPA). The amendment of the claim to recite that the seed comprises the recombinant DNA segment that was introduced into the parent plant would overcome the rejection.

Claim Rejections - 35 USC § 102

Claims 59-61, 63, 72 and 73 are rejected under 35 U.S.C. 102(e) as being anticipated by Verma et al. (U.S. Patent No. 5,639,950, issued June 17, 1997, filed June 29, 1994, having an effective filing date of September 29, 1992), for the reasons of record set forth in the office action mailed September 9, 2003.

Applicants' arguments filed March 15, 2004, have been fully considered but they are not persuasive.

Applicants argue that the Verma II patent (5,639,950) is not enabling for the transformation of monocots (brief page 5-6).

The Examiner maintains that the Verma II patent (5,639,950), and its parent Verma I (5,344,923), are both enabled for the transformation of monocots, because the transformation of monocots, including corn, was known and practiced in the art at the time of filing of Verma I. Furthermore, electroporation and biolistic-mediated methods for monocot transformation were known and practiced by August 1993, the effective filing date of Applicants' specification.

Applicants additionally argue that Verma II is effective only as of its June 1994 filing date for disclosure of "corn", since neither "corn" nor the synonymous terms "monocot"" or "maize"" appear in the priority application relied upon by Verma II (brief page 5-6). Applicants first point out that they noted in their response to the first Office Action that the current application claims priority to August 25, 1993 as a divisional application of U.S. Application Serial No. 08/599,714, filed January 19, 1996 (now U.S. Patent No. 6,281,411), which application was a continuation-in-part application of currently pending U.S. Application Serial No. 08/113,561, filed August 25, 1993, and that this grandparent application disclosed that transgenic monocot plants with drought resistance, including maize, can be prepared by expressing genes encoding a variety of osmotically active metabolites including proline. Applicants argue that the Verma II patent is effective only as of its June 1994 filing date for disclosure of "corn" and thus cannot anticipate the current claims. Applicants further argue that Verma I, on which the examiner relies for an effective filing date of September 29, 1992, is

insufficient, since a full text search of the Verma I patent on the USPTO patent database reveals that this patent does not include the terms "maize", "*Zea mays*" "corn" or "monocot" (brief pages 11-12).

Applicants' response to the first Office Action indicating that the current application claims priority to August 25, 1993 is acknowledged and is not disputed. Applicants' assertion that the Verma I patent does not include the terms "maize", "*Zea mays*" "corn" or "monocot" is also acknowledged and is also not disputed.

The Examiner maintains, however, that the Verma II patent is effective as of the filing date of its parent application for its claims directed to transgenic plants, including transgenic corn plants, because there is no substantial difference between the disclosure of the Verma II patent and the disclosure of its parent with respect to making and using plants transformed with a recombinant DNA encoding Δ^1-pyrroline-5-carboxylate synthetase. The Verma I patent discloses a recombinant DNA encoding Δ^1-pyrroline-5-carboxylate synthetase obtained from mothbean (Figure 1), and transgenic mothbean plants comprising said recombinant DNA, said transgenic plants exhibiting a 10 to 100 fold increase in proline in root tissue as compared to nontransformed wild-type plants (column 5 line 18-58). The Verma I patent claims recombinant DNA encoding Δ^1-pyrroline-5-carboxylate synthetase (columns 13-14). The Verma II patent discloses additional data pertaining to the same transgenic mothbean plants disclosed in the Verma I patent (column 6, line 47 through column 9, line 29 of Verma II); the disclosure of the Verma II patent regarding the method of obtaining transformed plants (column 6, lines 9-45 of Verma II) is IDENTICAL to the disclosure of Verma I (column 5, lines 18-46) regarding the method of obtaining transformed plants. The Verma II patent claims methods of transforming

plants to increase salt tolerance and drought resistance, as well as explicitly claiming transformed plants, including transformed corn plants (columns 17-18 Verma II). Because there is no substantial difference between the disclosure of the Verma II patent and the disclosure of its parent with respect to making and using plants transformed with a recombinant DNA encoding Δ^1-pyrroline-5-carboxylate synthetase, the Verma II patent claims directed to transgenic plants, including transgenic corn plants, are accorded the effective filing date of the parent application.

Applicants further argue that the rejected claims are drawn to a transgenic monocot plant which is substantially tolerant or resistant to a reduction in water availability, where the transgenic plant comprises a transgene encoding an enzyme catalyzing the synthesis of proline, whereas Verma I merely discloses the sequence of delta^1-pyrroline-5-carboxylate synthetase, making the sequence available to those of ordinary skill in the art who might discover a use for it, e.g., as Applicants have discovered a use in producing transgenic monocots expressing proline for drought resistance (brief page 12).

The Examiner maintains that the disclosure of Verma I is not limited to the disclosure of the sequence of delta^1-pyrroline-5-carboxylate synthetase. Verma I also discloses transgenic mothbean plants comprising said recombinant DNA, said transgenic plants exhibiting a 10 to 100 fold increase in proline in root tissue as compared to nontransformed wild-type plants (column 5 line 18-58). Verma I additionally discloses that it would be desirable to use genetic engineering of the proline production pathway in plants to counter osmotic stress to alter the level of a known osmoprotectant to thereby lead to a significant enhancement of crop performance under conditions of salt and drought stress (column 1 lines 43-48), that one object

of the invention is to provide a method to overproduce proline and thus increase sodium chloride and drought resistance in a plant by the introduction into the plant of the P5CS (delta^{1}-pyrroline-5-carboxylate synthetase) cDNA (column 2 lines 7-13), that regulation of the proline synthesis pathway in plants is exerted primarily at the P5CS step (column 4 lines 49-53), and that the invention demonstrates that it is possible to remove feedback control on proline production in plants and to produce the overexpression of proline from P5CS to confer salt and drought tolerance on a crop plant (column 5 lines 53-58). Furthermore, the Examiner maintains that Applicants have not discovered a use for the delta^{1}-pyrroline-5-carboxylate synthetase sequence, as Applicants' specification makes no reference to this enzyme, or to any sequence that encodes delta^{1}-pyrroline-5-carboxylate synthetase.

With regard to the Examiner's statement that plants disclosed by Verma I and/or II would inherently be substantially tolerant or resistant to a reduction of water availability, Applicants note that this statement directly contradicts the enablement rejection. Applicants argue that the Examiner cannot "have it both ways", and that in view of the comment by the Examiner admitting that a monocot transformed with the delta^{1}-pyrroline-5-carboxylate synthetase gene would inherently have a resistance to water availability, Applicants submit that the Examiner has acknowledged the enablement of the claims (brief pages 12-13).

Applicants' arguments directed to the rejection of the claims under 35 USC 112, first paragraph, are not germane to the instant rejection of the claims under 35 USC 102, as the different sections of the statute impose different requirements. See Hafner cited above. Furthermore, the statement that plants disclosed by Verma I and/or II would inherently be

substantially tolerant or resistant to a reduction of water availability does not contradict the enablement rejection, because the rejected claims are not directed to transformed plants which comprise a recombinant DNA segment encoding a delta[1]-pyrroline-5-carboxylate synthetase gene, and because the enablement rejection under 35 USC 112 was not solely predicated on the unpredictability of the ability of a recombinant DNA encoding delta[1]-pyrroline-5-carboxylate synthetase to confer tolerance or resistance to a reduction in water availability. The rejected claims are directed to transformed monocot plants that are substantially tolerant or resistant to a reduction in water availability, the cells of which comprise a recombinant DNA segment encoding any enzyme which catalyzes the synthesis of the osmoprotectant proline, and enablement rejection under 35 USC 112 was predicated on the general unpredictability of the ability of a recombinant DNA encoding any unspecified enzyme involved in proline biosynthesis to confer tolerance or resistance to a reduction in water availability. Accordingly the Examiner's assertion that a monocot transformed with the delta[1]-pyrroline-5-carboxylate synthetase gene would inherently have a resistance to water availability is not tantamount to acknowledging the enablement of the rejected claims, which are not directed to a monocot transformed with the delta[1]-pyrroline-5-carboxylate synthetase gene.

Applicants further argue that the Examiner's conclusion regarding inherency is flawed, as the Examiner has failed to provide any objective basis to support the enablement of the Verma I or Verma II reference. Applicants point out that the Examiner has failed to show that Verma I and/or II disclose a method for transforming monocots and teach transformation vectors that could be used to achieve gene expression in monocots. Applicants further argue that the

Examiner's unsupported allegations do not meet the relevant legal standards or the standards of the APA for maintaining a rejection, and that the Examiner is not allowed to bootstrap deficient references to support an anticipation rejection through unsupported allegations of inherency (brief page 13).

The Examiner's conclusion regarding inherency is not flawed, and the Examiner has provided objective basis to support the enablement of the Verma I and II. First, as discussed above, and at page 10 of the office action mailed September 9, 2003, Verma I and/or II need not disclose a method for transforming monocots and teach transformation vectors that could be used to achieve gene expression in monocots, because both Verma I and Verma II are enabled for the transformation of monocots, since the transformation of monocots was known in the art at the time of filing of Verma I.

Second, with respect to the Examiner's assertion that a monocot transformed with the delta[1]-pyrroline-5-carboxylate synthetase gene would inherently have a resistance to water availability, as discussed above, and at page 10 of the office action mailed September 9, 2003, Verma I discloses transgenic plants comprising a recombinant DNA encoding Δ^1-pyrroline-5-carboxylate synthetase (column 5 first full paragraph and Table 1), and Verma I teaches the use of Δ^1-pyrroline-5-carboxylate synthetase to increase proline content in transgenic plants as a means of enhancing osmotic stress tolerance (column 1 through column 2 fourth paragraph; column 5 second full paragraph). Furthermore, the transgenic plants disclosed in Verma I exhibit a 10 to 100 fold increase in proline in root tissue as compared to nontransformed wild-type plants (column Table 1). Finally, Verma II discloses additional data pertaining to increased salt tolerance and drought resistance of the same transgenic plants disclosed in Verma I (column 6,

line 47 through column 9, line 29 of Verma II), and claims methods of transforming plants to increase salt tolerance and drought resistance, as well as transformed plants, including transformed corn plants (columns 17-18).

Claim Rejections - 35 USC § 103

Claims 59-63 and 72-73 remain rejected under 35 U.S.C. 103(a) as being unpatentable over by Verma et al. (U.S. Patent No. 5,639,950) in view of Rayapati et al. (Plant Physiology, 1989, Vol. 91, pages 581-586) and in light of Applicant's admitted prior art, for the reasons of record set forth in the office action mailed September 9, 2003.

Applicants' arguments filed March 15, 2004, have been fully considered but they are not persuasive.

Applicants note that all elements of the claims have not been shown in the art and maintain that the rejection is insufficient on its face. Applicants argue that the Examiner has failed to show monocot plants in the prior art. Applicants maintain that the Examiner's assertion that Verma et al. teach corn, wheat barley, and rye monocot plants comprising a recombinant delta^{1}-pyrroline-5-carboxylate synthetase gene that catalyzes proline synthesis is unsupported and is baseless given that Verma does not even reference maize or monocot plants as of its effective prior date. Applicants also argue that Verma II has not even been demonstrated by the Examiner to be properly used as prior art. Applicants further argue that while Verma II claims a number of transgenic plant types, including maize, the reference does not disclose an actual transgenic monocot plant and thus does not cure the defect of Rayapati et al. Applicants further argue that the combined references do not teach fertile, transformed corn, and have not even been shown to

motivate a person of ordinary skill in the art to attempt to transform corn, let alone provide a reasonable expectation of success in doing so (brief pages 14-15).

The Examiner maintains that Verma II teaches corn, wheat barley, and rye monocot plants comprising a recombinant delta^{1}-pyrroline-5-carboxylate synthetase gene that catalyzes proline synthesis, and, as discussed above, that the Verma II patent claims directed to transgenic plants, including transgenic corn plants, are accorded the effective filing date of the parent application. This assertion is neither unsupported nor baseless, because Verma II in fact claims corn, wheat barley, and rye monocot plants comprising a recombinant delta^{1}-pyrroline-5-carboxylate synthetase gene (column 18 claims 13-16), including corn, wheat barley, and rye monocot plants with increased drought resistance and increased proline production (column 18 claims 14 and 15), and the claims of a U.S. patent are presumed to be valid. Furthermore, as discussed above, the Examiner maintains that both Verma I and Verma II are enabled for the transformation of monocots, because the transformation of monocots, including corn, was known and practiced in the art at the time of filing of Verma I. Finally, the Examiner maintains that Rayapati et al. would motivate one of ordinary skill in the art to transform a plant with a recombinant DNA encoding both a delta^{1}-pyrroline-5-carboxylate synthetase and a chloroplast transit peptide, because Rayapati et al. teach that native delta^{1}-pyrroline-5-carboxylate synthetase is localized in chloroplasts, and because DNA segments encoding amino terminal chloroplast transit peptides were known and used in the plant transformation art at the time of Applicants' invention.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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